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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/652,813	08/29/2003	Chi-Tang Ho	03-40155-US	2476

7590 07/02/2004

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EXAMINER

WITHERSPOON, SIKARL A

ART UNIT	PAPER NUMBER
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1621

DATE MAILED: 07/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<p align="center"><b>Office Action Summary</b></p>	<p><b>Application No.</b></p> <p>10/652,813</p>	<p><b>Applicant(s)</b></p> <p>HO ET AL</p>	
	<p><b>Examiner</b></p> <p>Sikarl A. Witherspoon</p>	<p><b>Art Unit</b></p> <p>1621</p>	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 11 February 2004.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-44 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4, 9-23 and 25-44 is/are rejected.
- 7) ☒ Claim(s) 3, 5-8 and 24 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>2/11/04</u> . | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is drawn to a benzotropolone derivative wherein substituents R1 to R3 may be a heterocyclic group selected from phenyl, benzyl, etc. However, a phenyl and benzyl are not heterocyclic, and as such, the claim is rendered indefinite. Claims 4 and 9 are drawn to a composition comprising a benzotropolone derivative as defined in claim 1 as the active ingredient; however, claims 4 and 9 depend on the benzotropolone of claim 1, which compound has substituents that render it indefinite, and as such, claims 4 and 9 are also indefinite.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Goodsall et al (US 6,113,965).

The compounds theaflavin, theaflavin-3-gallate, theaflavin-3,3'-gallate and theaflavin-3'-gallate, disclosed in figure 2, anticipate the instant claim.

Claim 1 is rejected under 35 U.S.C. 102(a) as being anticipated by Sang et al (Tetrahedron Letters, 2002).

Compounds 3 and 4 disclosed on page 7131 anticipate the instant claims.

Claims 27 and 28 are rejected under 35 U.S.C. 102(a) as being anticipated by Sang et al.

Sang et al disclose a process for preparing a benzotropolone derivative, wherein two tea catechins, epicatechin and epigallocatechin gallate are treated with horseradish peroxidase in the presence of hydrogen peroxide (see page 7129, second col.). The process disclosed therein anticipates the instant claims.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Lewis et al (Phytochemistry, 1998).

The reference discloses the compounds theaflavate B, isotheaflavin-3'-gallate, and neotheaflavin-3-O-gallate, on page 2512. These compounds anticipate the instant claims.

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Claims 1, 4, 9, 10, and 16 are rejected under 35 U.S.C. 102(a) as being anticipated by Liang et al (Nutrition and Cancer, 2002).

The reference discloses the compounds theaflavin, theaflavin-3-gallate, theaflavin-3'-gallate, and theaflavin-3,3'-gallate being used in as active ingredient in a composition to treat inflammatory skin edema (see p 218 and the table on page 220). This disclosure anticipates the instant claims.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lewis et al (Phytochemistry, 1998).

The instant claim is drawn to a specific benzotropolone derivative, i.e., neotheaflavin B. Lewis et al do not teach this specific compound; however, Lewis et al teach the compound theaflavate B (see page 2512) which is a stereoisomer of the compound of claim 2. The compounds differ in the planar position of the hydroxyl group on the heterocyclic ring.

The instant compound is rendered obvious since a person of ordinary skill would reasonably expect the stereoisomers to exhibit the same characteristics absent a showing or teaching of the contrary, i.e., that the isomer taught by Lewis et al does not

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produce the same antioxidant and/or anti-inflammatory effect as the isomer claimed herein.

Claims 11-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liang et al (Nutrition and Cancer, 2002).

The instant claims limit the method for treating an inflammatory condition, as recited in claim 10, to specific doses of the benzotropolone-containing composition, and to topical, oral, or parenteral administration of said composition.

Liang et al, as stated above in a rejection under 102(a), teaches benzotropolone derivatives as the active ingredient in compositions useful for treating inflammatory ear edema. Liang et al teach the application of said composition to the ear of a mouse having ear edema.

The difference between Liang et al and the present claims is that Liang et al do not expressly teach the specific dosage recited in the instant claims, nor the oral or parenteral administration of said composition.

Absent a showing that doses outside the range recited by applicants in the present claims would not effectively treat inflammatory conditions, the examiner purports that the doses recited by applicants would have been obvious to a person of ordinary skill, as one of ordinary skill would treat a patient affected with an inflammatory condition with a dosage that was found to have optimal anti-inflammatory efficacy. Furthermore, a person of ordinary skill would administer said composition to said

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affected patient using the mode of administration that was found most affective, i.e., orally, topically, or parenterally.

Claims 21-23, 25 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wiseman et al (Critical Review in Food Science and Nutrition, 1997).

The instant claims are drawn to a method for neutralizing free radicals in a patient, by administering to said patient an effective amount of a composition comprising a benzotropolone derivative as recited in claim 21, or epigallocatechin gallate (EGCG), at a concentration of at least about 0.5%.

Wiseman et al disclose a method for neutralizing reactive oxygen species (ROS) and free radicals in a patient using tea antioxidants, such as epicatechin, epigallocatechin, epigallocatechin gallate, and theaflavins (see page 709, and table 1 on same page).

The difference between Wiseman et al and the present invention is that Wiseman et al do not expressly teach the concentration of said compounds when used as antioxidants.

However, the examiner takes the position that it would have been obvious to a person of ordinary skill, at the time the present invention was made, to modify the concentration of the antioxidant compounds in order to obtain the concentration that affords optimal antioxidant activity in a patient in need of such compounds. Accordingly, the instant claims are rendered obvious.

Claims 29-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sang et al (Tetrahedron Letters, 2002) and further in view of Goodall et al (US 6,113,965).

The instant claims limit claim 27 to specific reactants used in synthesizing a benzotropolone derivative, as per claim 27.

Sang teaches epicatechin and epigallocatechin gallate being reacted to produce the corresponding benzotropolone derivative, but does not teach the other catechins recited in the instant claims as reactants.

Goodsall et al, however, teach several theaflavins that are produced from the corresponding catechin(s) and/ or gallates.

Since, as suggested by Goodsall et al, several different catechins are found in tea leaves, including epicatechin and epigallocatechin gallate, as taught by Sang et al, it would have been obvious to a person of ordinary skill in the art to substitute the compounds taught by Sang et al with one or more of the compounds taught by Goodsall et al. A person of ordinary skill in the art would have been motivated to make such a substitution in order to produce the benzotropolone derivative having the desired substituents using the oxidation process taught by Sang et al, since the compound taught by Goodsall et al are known prerequisite compounds in synthesizing various theaflavins (benzotropolone derivatives).



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Claims 3, 5-8 and 24 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sikarl A. Witherspoon whose telephone number is 571-272-0649. The examiner can normally be reached on M-F 8:30-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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